

Application No. 10/081,118

New Docket No.: 22321-00002-US1
Old Docket No.: 20198-00059**REMARKS**

Claims 3-6 and 9-21 were pending in the application. Claims 22-25 were added. Claims 12-18 were withdrawn and are canceled. Thus, claims 3-6, 9-11 and 19-25 are currently pending.

Entry of this amendment is kindly requested.

In order to more fully put the application in condition for allowance, Applicant respectfully requests that the withdrawn claims 12-18 be canceled without prejudice or disclaimer. Applicants reserve the right to refile the canceled claims in a separate application.

Telephonic Interview

Applicants thank Examiner Gabel for the opportunity to have a short telephonic interview on April 19. In the interview, the rejections of claims 19 and 20 under 35 USC § 112 were clarified. Agreement was reached that recitation of "nucleated blood cells" was sufficient to inherently provide antecedent basis for the phrase "the nucleic acids." Further agreement was reached that antecedent basis was proper in claim 20.

Rejections under 35 USC §112

Claims 5, 19 and 20 stand rejected for indefiniteness.

Claim 5 has been amended to be substantially in accord with Examiner's suggested revision.

In view of the amendment of claim 5 and the results of the telephonic interview, withdrawal of the rejections of claims 5, 19 and 20 under 35 USC § 112 is respectfully requested.

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New Docket No.: 22321-00002-US1
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Applicants note that rejections under 35 USC § 102 over Sakata or over Deka have been withdrawn by the Examiner.

Rejections Under 35 USC § 103

Claims 3-6, 9-11 and 19-21 stand rejected as obvious over Sakata (US 5,496,734) in view of Haas et al., (Abstract). Sakata discloses a reagent according to Examiner Gabel, for identifying, counting and classifying blood cells. The reagent comprises a lysing agent which is quaternary ammonium salts at a concentration that lyses erythrocytes and a fluorescent stain that can permeate through permeabilized cell membranes of nucleated unlysed cells (leucocytes) so as to incorporate with and label intracellular nucleic acids of the unlysed nucleated cells. The Examiner states that Sakata et al. differs from the instant invention in failing to teach incorporation of ionophor into a reagent for identifying and counting nucleated blood cells.

According to the Examiner: "Haas et al. provide use of valinomycin in a cation-anion cotransport, as an ionophore for increasing permeability of cell membrane in red blood cells to specific elements, i.e., sodium and potassium. Haas et al. show investigations of valinomycin with different cells and successfully demonstrated that there is electroneutrality of $(\text{Na}^+ + \text{K}^+ + 2\text{Cl}^-)$ cotransport in MDCK cells."

Moreover, the Examiner states that it "would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate valinomycin as an ionophore as taught by Haas et al., into the reagent taught by Sakata for use in identifying, counting and classifying blood cells because Haas specifically provided that valinomycin is capable of increasing permeability of cell membrane in red blood cells; hence enhancing penetration of stain into the intracellular red blood cell environment to thus allow more accurate detection, identification, and classification of nucleated blood cells in a sample."

In distinction to the Examiner's characterization of Haas et al., the reference never describes or suggests that valinomycin is an agent that promotes the penetration of the stain into

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cells to be marked. Rather, Haas et al. notes that "valinomycin has been used successfully to demonstrate the electroneutrality of (Na⁺ + K⁺ + 2Cl⁻) cotransport in MDCK cells." Haas et al. at line 24 of the Abstract. Demonstration of electroneutrality of small ion transport is not remotely the same as showing an increase in permeability to a nucleic acid stain which are larger and more complex molecules than the simple ions that Haas described.

Haas et al. also report that valinomycin was used to measure electrogenicity or electro neutrality of Na⁺, K⁺, and Cl⁻ ion transport, in particular in use in red blood cells. *Id.* at l. 10 and l. 20. Unlike Haas et al. the invention as claimed, uses valinomycin or other ionophore as part of a composition and method to increase the permeability of cells to a nucleic acid stain. Haas et al. does not suggest that an ionophor could increase permeability of a cell to a nucleic acid stain.

Thus, Haas et al. does not provide the elements of the claim that are missing in Sakata.

Moreover, Sakata does not provide motivation to combine the method with a reference disclosing use of an ionophore. Haas et al. does not provide motivation to combine with a reference showing a lysing reagent and fluorescent stain.

For at least these reasons, the combination of references does not render the claims obvious. Allowance of the claim is respectfully requested.

No new matter has been added. Support for amended claim 5 is found in the application as a whole. In particular, support for amended claim 5 is found on p. 8, ll. 5-8. Support for new claims is found on p. 7, l. 21, on p. 9, ll. 31-33, p. 10, l. 1, and elsewhere.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Although no fees are believed due with this response, Applicants hereby authorize the Commissioner to please charge our Deposit Account No. 22-0185, under Order No. 22321-00002-US1 for any fees deemed necessary, from which the undersigned is authorized to draw.

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Respectfully submitted,

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